REMARKS

Claims 40-42, and 50-56 are currently pending and non-elected Claims 57-60 have been reclassified from "Withdrawn" to "Canceled" as requested by the Examiner. The Applicants respectfully acknowledge the Examiner's withdrawal of the previous §102 and §112 rejections. Nonetheless, the Examiner presents a new rejection based upon obviousness:

I. Claims 40-42 and 50-56 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over US Patent No. 6,067,467 To John.

I. The Claims Are Not Obvious In View Of John

Obviousness is currently determined based upon an evaluation of the magnitude of the differences between the claimed embodiment and the asserted prior art:

> In Graham v. John Deere Co. of Kansas City, 383 U.S. 1, 86 S. Ct. 684, 15 L. Ed. 2d 545 (1966), the Court set out a framework for applying the statutory language of § 103 ... "Under § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained ...

KSR v. Teleflex, 127 S. Ct. 1727, 1734 (2007). Further, the *KSR* holding only cautioned against a strict application of the "teaching-suggestion-motivation test" such that an explicit teaching is not required to be found within the cited applications. Consequently, it is still required to: i) establish some motivation to combine the references either explicitly or implicitly, and ii) establish a *prima facie* case of obviousness, wherein the prior art reference (or references when combined) must teach or suggest all the claim limitations with a reasonable expectation of success. *In re Vaeck*, 947 F.2d 488, 20 USPQ.2d 1438 (Fed. Cir. 1991); and *MPEP § 2142*; Establishing A *Prima Facie* Case Of Obviousness. The Applicants submit that the Examiner has not made a *prima facie* case of obviousness.

A. John Does Not Teach All The Elements

The Examiner states that:

> Initial EEG measurement may be taken while the patient is awake and before the anesthesia is administered (*note that the anesthesia is the drug that is being administered*) (column 4, lines 42-44).

Office Action, sentence bridging pg 3 – 4 [emphasis in original]. The Applicants' disagree because, when viewed in its complete context, the Examiner's above cited passage refers to an EEG measurement that is not the "reference or baseline EEG". First, the Examiner's cited passage teaches that a pre-anesthesia EEG measurement is not necessary:

> *Preferably*, but not necessarily, initial EEG measurements are taken while the patient is awake, before the anesthesia is administered.

John col. 4 ln 42-44 [emphasis added]. Second, John clearly teaches that the pre-anesthesia EEG documents the patient's "awake state" and is followed by a post-induction EEG measurement to create the "reference or baseline" EEG to which further EEGs are compared:

> Measurement of the patient's brain waves preferably begins a few minutes before the anesthetic is administered. This provides data of the patient's awake state to the system.
>
> The anesthesiologist will then administer an anesthetic, generally gas, to the patient until the patient has attained the desired plane of anesthesia ... The patient's brain waves, at that point, are collected, analyzed and become a self-norm ("reference"). In theory, if the patient's brain waves are correctly analyzed and remain, during the operation, within a band ("reference band") close to the reference, the patient should remain at the same desired plane of anesthesia. Depending on the direction of movement of the analyzed brain waves, if outside of the reference band, either more or less anesthesia should be administered, or oxygen should be administered.

John, col 2 ln 49-67 [emphasis added], and

> At regular intervals after this baseline is established ... a statistically adequate EEG and EP sample is ... compared to the baseline ...

John col. 5 ln 7-10 [emphasis added], and

> All of these various [EEG] features are then compared against the "baseline" (data collected from the pre-operative patient after being anesthetized).

John, col 9 ln 19-21 [emphasis added]. The Applicant's submit that John clearly compares a first post-induction EEG tracing to a second post-induction EEG tracing to monitor anesthesia level. John does not compare a pre-induction EEG tracing to a post-induction EEG tracing to monitor anesthesia level.

Nonetheless, without acquiescing to the Examiner's argument but to further the prosecution, and hereby expressly reserving the right to prosecute the original (or similar) claims, Applicants have amended Claims 40 and 54 to recite that the first EEG is from a patient that is "drug and medication free". *See, Applicants' Specification, pg 25 ln 2-3.* The Examiner is also requested to note that the Applicants have voluntarily amended Claims 41-42 and 55-56 to improve clarity and proper antecedent basis. This amendment is made not to acquiesce to the Examiner's argument but only to further the Applicants' business interests, better define one embodiment and expedite the prosecution of this application.

John fails to teach EEG measurements from a "drug and medication free" patient. In fact, all EEG's measured in John are taken when the patient is at least sedated (i.e., after the administration of at least one drug or medication) whether using; i) a normative database; ii) a pre-induction patient; or iii) a post-induction patient baseline:

> ... the realtime analysis of the data and updated comparisons of features extracted from that data to *a normative database* constructed from a population of surgical patients sedated but awake prior to induction of anesthesia, the *pre-induction* but sedated state of the patient and the *patient's baseline* after induction of anesthesia ("self-norm")..

John col. 8 ln 28-34 [emphasis added]. The Applicants submit that John does not teach a comparison of a 'drug and medication free EEG' to a 'post drug administration EEG' wherein the difference between the two EEGs determines drug efficacy.

The Examiner is respectfully requested to withdraw the present rejection.

B. John Provides No Motivation To Successfully Create The Applicants' Embodiment

The Examiner states that the Applicants' claimed embodiment is allegedly obvious because:

> The system of John compares a first set of data from the patient before anesthesia is administered and a second set of data after the plane of anesthesia is attained ... Column 13, lines 1-14).

Office Action, sentence bridging pg 4-5. The Applicants disagree and respectfully point out that the Examiner is mistaken because the full scope and content of John has not been properly considered. Further, when John's scope and content is properly considered the reference does not provide any motivation to one having ordinary skill in the art to successfully create the Applicant's embodiment.[1] Specifically, the Examiner's above quotation is not related to the collection of quantitative electroencephalographic data, but to the collection of electromyographic data:

> In addition to the EEG electrodes an EMG (electromyograph) electrode 70 may be used at a frontal scalp location. The EEG electrodes at the front of the scalp, when they detect energy in the Beta 2 band (25-50 Hz) are detecting facial muscle activity and are acting as an EMG electrode. The operator can determine, in order to arrive at a proper plane of anesthesia, using the frontal electrodes in the Beta 2 band or/and the EMG electrode 70 if there is too much muscle activity (indicating insufficient anesthesia). *The system compares a first set of data from the patient before anesthesia is administered and a second set of data after the plane of anesthesia is attained* ... In each case the first and second sets of data consist of data from the EMG electrode 70 and/or frontal EEG electrodes.

[1] These are requirements under the *Graham* elements to show obviousness.

John, col 12 ln 59 - col 13 ln 9 [emphasis added]. Clearly, the Examiner has overlooked the fact that John is referring to the measurement of muscle activity by collecting and analyzing electromygraphic (EMG) data using either EMG electrodes and/or a specific EEG electrode.

Nonetheless, without acquiescing to the Examiner's argument but to further the prosecution, and hereby expressly reserving the right to prosecute the original (or similar) claims, Applicants have amended Claims 40 and 54 to recite that the first EEG measurement excludes "paroxysmal events":

> The conventional EEG was reviewed to exclude paroxysmal events, spikes, sharp waves, focal disturbances and other abnormalities …

Applicant's Specification, pg 43 ln 1-2 [emphasis added]. The Examiner is requested to note that the Applicant's definition of "paroxysmal events" includes muscle activity measurements:

> A "paroxysmal event" is a brief sudden disturbance in the background EEG, often consisting of short duration spikes and waves, which are often but not always accompanied by a sudden voluntary or involuntary muscle movement.

Applicant's Specification, pg 8 ln 13-15 [emphasis added]. This amendment is made not to acquiesce to the Examiner's argument but only to further the Applicants' business interests, better define one embodiment and expedite the prosecution of this application.

As such, the Examiner's argument is not relevant to the Applicants' presently claimed embodiment and one having ordinary skill in the art would not be motivated to use EMG signals to perform QEEG analysis. The Examiner is respectfully requested to withdraw the present rejection.

C. "Drug Amount" Does Not Predict "Drug Efficacy"

While a *prima facie* case of obviousness requires a substantive elemental framework (i.e., teaching all the elements and/or providing a motivation for success), it should be noted that

obviousness is also not present when the claimed combination of elements are unpredictable (i.e., that which has not been considered likely by one skilled in the art);

> … a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions.

KSR v. Teleflex, 127 S. Ct. 1727 (2007). The Applicants provide evidence below that John does not make the Applicants' claimed embodiment predictable.

The Examiner states that John makes the Applicants' claimed embodiment allegedly obvious because:

> The system monitors drug efficacy because it detects if there is a low mean total EEG power, if there is too little anesthesia, and if there is too much anesthesia (column 13, lines 50-64).

Examiner's Action, pg. 5. The Applicants' disagree because: i) John does not even mention the term "drug efficacy"; and ii) when considered in full context, the Examiner's cited passage explains that an observation of 'low mean total EEG power' is a warning of potential anesthetic overdose:

> Such low total EEG power arises from burst suppression, indicating too much anesthesia.

John, col 13 ln 52-54. Rather than monitoring "drug efficacy", John explains that the method solves problems related to titrating a proper "drug amount" to maintain a steady state anesthetic response:

> It has been suggested that some of these problems would be avoided by having a computer system determine the best anesthetic mix and the amount of each anesthetic based on the patient's sex, age, weight, physical condition and the type of operation.

John, col 2 ln 7-13 [emphasis added]. As such, the Examiner has not fully considered the scope and content of John, and has not explained how the known technical differences

between "drug efficacy" and "drug amount" fail to differentiate between the Applicant's claimed embodiment.[2] Here, the Examiner is improperly defining "drug efficacy" in terms of whether the amount of a drug administered to a person is sufficient to elicit a desired response. One having ordinary skill in the art would consider the term "efficacy" related to the relative potency of a drug, and not for titrating a steady state response of a single drug:

> efficacy (ef'i-k?-se) the ability of a drug to achieve the desired effect.
>
> Dose-effect curve for two drugs of different efficacy: The efficacy of drug *A* is greater than that of drug *B*. the degree to which an intervention accomplishes the desired or projected outcomes.

Dorland's Medical Dictionary, merck.source.com. As described in detail above, there are very large differences between comparing two EEGs taken after a drug has been administered (as described by John) and comparing a pre-drug EEG to a post-drug EEG (as described by the Applicants). In John's approach, the goal is to use the second EEG to show that a drug is having the same effect as observed during the first EEG. In the Applicants' approach, the goal is to use the second EEG to show that a drug is having a different effect as observed during the first EEG.

The Applicants submit that John does not make the Applicants' claimed embodiment obvious because methods that monitor "drug amount" do not have predictive value for methods that identify "drug efficacy". The Examiner is respectfully requested to withdraw the present rejection.

II. John Does Not Teach Clinical Or Therapeutic Outcomes

In addition to the arguments presented above in rebutting the Examiner's obviousness rejection against Claim 40, the Applicants further clarify the elected subject matter within this application by presenting new Claim 61. New Claim 61 recites that "drug efficacy" is correlated with improved clinical outcome that may be determined by

[2] The is also a requirement under the *Graham* elements to show obviousness.

identifying particular EEG biomarkers (i.e., for example, multivariate outcome measurements):

> Current behavioral definitions of psychiatric disorders do not correlate well with response patterns to medical treatment. Since psychiatric imbalances are behaviorally defined, they do not demonstrate a consistent relation with individual neurophysiological information, such as from EEG/QEEG or other neurophysiological technques such as MRI, FMRI, PET, SPECT or other related techniques. However, if neurophysiological information were used as the independent variable and medication response is analyzed as the dependent variable, a connection between neurophysiology and the clinical outcome of treatment may be observed.

Applicant's Specification pg 2 ln 10-17. This embodiment employs the use of clinical outcome measurements including Clinical Global Improvement (CGI) scores[3], Hamilton-D (HAM-D) scores[4], and (BECK) scores[5]. These measurements of clinical improvement are correlated with electroencephalographic outcome measurements in patients with an improved clinical response:

> Outcome prediction from EEG/QEEG information correlated with symptomatic behavioral assessments - CGI ratings, HAM-D and BECK scores.

Applicants' Specification, pg 48 ln 28-29 and Example I in general. In support of Applicantsd dependent Claims 63 and 64, the Applicant's specification teaches that statistically significantly HAM-D and BECK test scores is an indicator of drug efficacy:

> These changes in test scores between the two treatment groups are highly significant (Friedman ANOVA $\chi 2(N=13;\ df = 63)\ p < 0.009$).

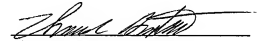
[3] See, Applicants' Specification pg 34, ln 3-12.
[4] See, Applicants' Specification pg 46 ln 24-32.
[5] See, Applicants' Specification pg 46, ln 24-32.

Applicant's Specification, pg. 46, ln 30-32. The Applicants respectfully request the Examiner to pass these new claims to allowance in conjuction with Claims 40-42, and 50-56.

CONCLUSION

The Applicants believe that the arguments and claim amendments set forth above traverse the Examiner's rejections and, therefore, request that all grounds for rejection be withdrawn for the reasons set above. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, the Applicants encourage the Examiner to call the undersigned collect at 781.828.9870.

Dated: January 21, 2009



Thomas C. Howerton
Registration No. 48,650

MEDLEN & CARROLL, LLP
101 Howard Street, Suite 350
San Francisco, California 94105
781.828.9870